UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte RIYI SHI and RICHARD B. BORGENS

Appeal 2007-0289
Application 09/438,206
Technology Center 1600

Decided: December 3, 2007

Before TONI R. SCHEINER, DONALD E. ADAMS, and NANCY J. LINCK, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134 involves claims 22-30, 38-40, 43, and 44, the only claims pending in this application. We have jurisdiction under 35 U.S.C. § 6(b).

INTRODUCTION

The claims are directed to a method of treating a mammalian patient having suffered an injury to its spinal cord. Claims 22 and 30 are illustrative:

22. A method of treating a mammalian patient having suffered an injury to its spinal cord, said method comprising contacting the injured spinal cord after the injury but within a period no greater than about 24 hours after said injury with a composition comprising an effective amount of at least one C1-C10 polyalkylene glycol, wherein the effective amount of at least one C1-C10 polyalkylene glycol is effective to restore nerve impulse conduction through said injured spinal cord.

30. The method according to claim 22, wherein said polyalkylene glycol is polyethylene glycol and wherein said method further comprises the step of contacting said injured spinal cord with a synergistic amount of 4-aminopyridine and within an effective time of contacting said spinal cord with said polyethylene glycol so as to produce a synergistic increase in restoration of nerve function and reflex behavior in said patient.

The Examiner relies on the following prior art references to show unpatentability:

Edwards	US 4,369,769	Jan. 25, 1983
Shulman	US 4,599,354	Jul. 8, 1986
Balasubramanian	US 5,382,584	Jan. 17, 1995

Selby, "Correspondence," *Neurosurgery* 12(5):591 (1983).

Potter, "Aminopyridine: Six Years Experience and Progress in Spinal Cord Injury," *Clin. Invest Med.* 19(4):S80, Abstract No. 533 (2000).

The rejections as presented by the Examiner are as follows[1]:

1. Claims 22-30, 38, 40, and 44 stand rejected under the enablement provision of 35 U.S.C. § 112, first paragraph.

2. Claims 22, 24-30, 38-40, 43, and 44 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Balasubramanian and Potter.

3. Claims 22-30, 38-40, 43, and 44 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Shulman and Edwards.

We reverse rejection 1 and rejection 2. As to rejection 3, we affirm the rejection of claims 22-39, 38, 39, and 44; and reverse the rejection of claims 30, 40, and 43.

DISCUSSION

Claim interpretation:

Claim 22 is drawn to a method of treating a mammalian patient that has suffered an injury to its spinal cord. The method comprises the single step of contacting the injured spinal cord with a composition comprising an effective amount of at least one C1-C10 polyalkylene glycol, e.g., polyethylene glycol (PEG) (Specification 3: 7-9; claim 38).

The claim, however, places two requirements on this single method step. Specifically, the injured spinal cord must be contacted with

[1] According to the Examiner, "the outstanding provisional obviousness double patenting [rejection] is maintained while the terminal disclaimer filed November 23, 2005 [is] being processed. Once the terminal disclaimer is approved, the obviousness double patenting rejection will be withdrawn" (Answer 3). The record reflects that this terminal disclaimer was approved (Paper entered into the record August 25, 2006). Accordingly, it is our understanding that the outstanding provisional obviousness-type double patenting rejection has been withdrawn and is not before us on appeal.

1. the composition within a period no greater than about 24 hours after the injury; and

2. an amount of at least one C1-C10 polyalkylene glycol that is effective to restore nerve impulse conduction through the injured spinal cord.

Claims 23-30 depend, directly or indirectly, from claim 22. Claim 38, the only other independent claim, is similar to claim 22 with the only exception being that the composition comprises an effective amount of PEG, instead of at least one C1-C10 polyalkylene glycol. Claims 39, 40, 43, and 44 depend, directly or indirectly, from claim 38.

Enablement:

Claims 22-30, 38, 40, and 44 stand rejected under the enablement provision of 35 U.S.C. § 112, first paragraph. The Examiner finds that Shelby observed that PEG having a molecular weight of 4000 daltons causes "dissolution of myelin and may cause manifestation of the loss of neural function" (Answer 4). Accordingly, the Examiner finds that while Appellants' Specification provides an enabling description of the use of "PEG with a molecular weight of 40 [sic[2]] to 3500 daltons," Appellants' Specification does not provide an enabling description of the use of PEG 4000.

In response, Appellants assert that Selby's observations "of the dissolution of myelin, and concerns of a possible loss of neural function with

[2] The Examiner's reference to PEG having a molecular weight of 40 daltons appears to be a typographical error. It appears that the Examiner is referring to Appellants preferred polyalkylene glycol molecular weight which is from about 400 to about 3500 daltons (Specification 12: 4-6).

the application of Depro-Medrol containing PEG 4000, do not reasonably establish a lack of enablement for the use [of] PEG 4000" in Appellants' claimed methods (Br. 6). According to Appellants,

> [t]he Specification teaches that "a wide range of molecular weights of polyalkylene glycols may be used" (page 12, lines 4-5 of the Specification) and that "a physiological, balanced media and the aforementioned PEG solution is all that is required to produce functionally significant repair in mammalian spinal cords" (page 27, lines 3-5 of the Specification). Moreover, the Specification teaches that "no specific PEG molecular weight [is] critical to the process," (page 27, lines 7-8 of the Specification), with PEG solutions of 400, 1400, 1800, 2000, and 3700 daltons producing functionally significant repair in injured mammalian spinal cords (page 27, lines 3-9 of the Specification), and functional fusion results obtained using 1400, 1800, 2000, and 3500 dalton PEG (page 31, lines 28-31 of the Specification).

(*Id.*)

The Examiner bears the initial burden of providing reasons why a supporting disclosure does not enable a claim. *In re Marzocchi*, 439 F.2d 220, 223 (CCPA 1971). Once the Examiner has established a reasonable basis to question the enablement provided for the claimed invention, the burden shifts to Appellants to show that one of ordinary skill in the art could practice the claimed invention without undue experimentation. *Id.* In this regard, we note that inoperative embodiments do not necessarily invalidate the claim. *See Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1576-77 (Fed.Cir.1984); *In re Cook*, 439 F.2d 730, 735 (1971) (noting that although claims may read on some inoperative embodiments, this does not necessarily invalidate the claim if the necessary information to limit the claims to operative embodiments is known to a person of ordinary

skill in the art). The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation "must not be unduly extensive." *Atlas Powder*, 750 F.2d at 1576. The Patent and Trademark Office Board of Appeals summarized the point well when it stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Ex parte Jackson, 217 USPQ 804, 807 (BPAI 1982), *quoted with approval in In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) .

Accordingly, the issue before us is whether evidence of one potentially inoperative embodiment is sufficient to sustain a rejection of the claimed genus.

While the Examiner recognizes that "inoperative embodiments are excluded by language in a claim" and "[t]he presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled," the Examiner maintains the rejection because the "operable embodiments disclosed in the instant specification are all under molecular weight of 4000 [d]altons" (Answer 10). We are not persuaded.

The independent claims require that the active agent, at least one C1-C10 polyalkylene glycol (claim 22) or PEG (claim 38), is effective to restore nerve impulse conduction through the injured spinal cord. Thus, as required by the claims before us on appeal, the active agents must be capable of restoring at least some nerve impulse conduction through the injured spinal

cord. Those agents that are not capable of performing this function are therefore excluded from the scope of the claim. As Appellants explain (Br. 6), the Specification provides examples of the tests used to determine the effectiveness of compounds within the scope of their claims and have specifically disclosed that "PEG solutions of 400, 1400, 1800, 2000, and 3700 daltons produc[e] functionally significant repair in injured mammalian spinal cords (page 27, lines 3-9 of the Specification), and functional fusion results obtained using 1400, 1800, 2000, and 3500 dalton PEG (page 31, lines 28-31 of the Specification)" (*id.*). The Examiner has not explained why it would require undue experimentation to perform these tests with C1-C10 polyaklylene glycol or PEG regents of varying molecular weight to determine whether they would be effective to restore nerve impulse conduction through an injured spinal cord as required by the claimed invention.

On reflection, we find that the weight of the evidence falls in favor of Appellants. Accordingly, we reverse the rejection of claims 22-30, 38, 40, and 44 stand rejected under the enablement provision of 35 U.S.C. § 112, first paragraph.

Obviousness:

Balasubramanian and Potter:

Claims 22, 24-30, 38-40, 43, and 44 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Balasubramanian and Potter. The Examiner finds that Balasubramanian teaches a method of treating spinal cord injuries with piperazinyl phenylacetamide compounds (Answer 6). The Examiner finds that Balasubramanian's piperazinyl

phenylacetamide compounds are formulated into solution or suspension with a solvent such as PEG 200-1500 (*id.*). From this the Examiner reasons that since Balasubramanian exemplifies the use of PEG to dissolve the piperazinyl phenylacetamide compounds (Answer 8), "[o]ne of ordinary skill in the art would have been motivated to administer the piperazinyl phenylacetamide with polyethylene glycol 200-1500 . . . in a method to treat spinal cord injuries . . ." (Answer 7).

The Examiner relies on Potter to teach "the use of 4-aminopyridine to treat spinal cord injury . . ." (Answer 7). According to the Examiner, since "4-aminopyridine is known to be useful as [a] treatment for spinal cord injury," "[o]ne of ordinary skill in the art would have been motivated to employ 4-aminopyridine with the piperazinyl phenylacetamide compounds of Balasubramanian to treat spinal cord injuries" (Answer 7). Potter makes no reference to a composition comprising a C1-C10 polyalkylene glycol.

In response, Appellants do not dispute that Balasubramanian teaches a method wherein the spinal cord is contacted, intrathecally, with a composition comprising PEG within a period no greater than about 24 hours after spinal cord injury. Appellants also do not argue that a spinal cord injury that is within the scope of their claimed invention is distinct from what Balasubramanian characterizes as a spinal cord injury. Instead, Appellants assert that Balasubramanian only teaches the use of PEG as a lubricant or a vehicle for the parenteral administration of an active compound (Br. 11; Reply Br. 8). According to Appellants, Balasubramanian "does not teach the administration of *an effective amount* of polyethylene glycol, *wherein the effective amount of* polyethylene glycol *is effective to*

restore nerve impulse conduction through said injured spinal cord" (Br. 12; Reply Br. 8).

The Examiner does not dispute that Balasubramanian fails to teach the effect of PEG on an injured spinal cord. Nevertheless, the Examiner's reasoning appears to be that since Balasubramanian teaches the use of PEG as a solvent for the active ingredient in a composition, by contacting an injured spinal cord with a composition comprising PEG, a person of ordinary skill in the art will necessarily contact the injured spinal cord with an amount of a C1-C10 polyalkylene glycol.

Therefore, the dispositive issue is whether the combination of Balasubramanian and Potter teaches a method wherein an injured spinal cord is contacted with an amount of at least one C1-C10 polyalkylene glycol, or PEG, that is effective to restore at least some nerve impulse conduction through the injured spinal cord.

Appellants define PEG as a biomembrane fusion agent (Specification 12: 11-12). According to Appellants' Specification, while "the percentage by weight of the fusion agent in the composition may vary, the composition typically includes at least about 40% of the fusion agent by weight" (Specification 12: 20-22).

Balasubramanian teaches that the "invention pertains to N-piperazineacetamide derivatives of 4,5-diphenyl-oxazoles, thiazoles and imidazoles having drug and bio-affecting properties and to their preparation and use" (Balasubramanian, col. 1, ll. 15-18). Balasubramanian refers to these compounds as having the structure depicted by Formula I (Balasubramanian, col. 2, l. 40 through col. 3, l. 15). Balasubramanian teaches a composition comprising compounds of formula I compound or one

of its salt forms in water or a vehicle consisting of a polyhydric aliphatic alcohol such as glycerine, propylene glycol, and *the polyethylene glycols* or mixtures thereof" (Balasubramanian, col. 6, ll. 18-23). According to Balasubramanian, "the polyethylene glycols consist of a mixture of non-volatile, usually liquid, polyethylene glycols which are soluble in both water and organic liquids and which have molecular weights from about 200 to 1500" (Balasubramanian, col. 6, ll. 23-27).[3]

Therefore, when Balasubramanian's compounds having the structure of Formula I are dissolved in the PEGs, the composition used in Balasubramanian's method falls within the scope of the composition set forth in Appellants' claimed invention. The problem, however, is that Balasubramanian does not offer a preference for PEG over any other of the other reagents taught by Balasubramanian that are suitable as a vehicle for the compounds of formula 1. A person of ordinary skill in the art could select water or glycerine, propylene glycol, and the PEGs or mixtures thereof to solubilize Balasubramanian's compounds having Formula I. It is, however, only when a person of ordinary skill in the art selects PEGs that one would obtain the additional benefit of restoring nerve impulse conduction through an injured spinal cord.

Balasubramanian and Potter fail to appreciate that any of their compounds, much less PEG, would be effective in restoring to any extent nerve impulse conduction through an injured spinal cord. In the absence of some guidance for the selection of PEG, we cannot agree with the Examiner's conclusion that a person of ordinary skill in the art at the time

[3] According to Appellants, while polyalkylene glycols of molecular weight of about 400 to about 3500 daltons are preferred, a wide range of molecular weight polyalkylene glycols may be used (Specification 12: 4-6).

the invention was made would have concluded that Appellants' claimed method is encompassed by, or more simply just the discovery of a new benefit of the process taught by Balasubramanian alone or in combination with Potter. *Cf. In re Woodruff*, 919 F.2d 1575, 1578 (Fed. Cir. 1990).

For the foregoing reasons, we find that the combination of Balasubramanian and Potter fails to teach or suggest a method wherein an injured spinal cord is contacted with an amount of at least one C1-C10 polyalkylene glycol, or PEG, that is effective to restore nerve impulse conduction through the injured spinal cord. Accordingly, we reverse the rejection of claims 22, 24-30, 38-40, 43, and 44 stand rejected under 35 U.S.C. § 103 as being unpatentable over the combination of Balasubramanian and Potter.

Shulman and Edwards:

The combination of Shulman and Edwards stands on a different footing. Claims 22-30, 38-40, 43, and 44 stand rejected under 35 U.S.C § 103(a) as unpatentable over the combination of Shulman and Edwards. Appellants provide separate arguments for claims 30, 40, and 43. Accordingly, we discuss the claims as they relate to the following two groups: I. claims 22-29, 38, 39, and 44; and II. claims 30, 40, and 43. We select claims 22 and 30 as representative of the two groups.

The Examiner finds that Shulman teaches a pain relief composition comprising "2.3% of PEG . . ." (Answer 8). More specifically, Shulman teaches a pain relieving composition comprising the active agent, n-butyl-p-aminobenzoate and a suspending agent (Shulman, col. 2, ll. 15-22). According to Shulman, the suspending agent "should have a relatively high

molecular weight, greater than 1,000 (e.g., 1000-5000)," is preferably PEG, and is typically present in a concentration of up to 10 wt. % based on the total weight of the suspending agent and water in the aqueous carrying medium (Shulman, col. 5, ll. 7-10; col. 6, ll. 55-66).

Shulman teaches that the suspension "produces lasting pain relief in a body region by injection of the suspension around a nerve proximal to a body region where pain relief is desired" (Shulman, col. 3, ll. 11-14). According to Shulman, "[t]he butyl aminobenzoate is released sufficiently slowly to provide just enough anesthetic action to block pain sensation traveling through the nerves in the body region while leaving intact most other nerve conduction functions" (Shulman, col. 3, ll. 19-23). Shulman exemplifies the use of a composition comprising 2.3% PEG as an epidural injection (Shulman, col. 3, l. 28 - col. 4, l. 16).

While Shulman teaches that this PEG-containing composition is effective to treat pain, as the Examiner recognizes, Shulman does not teach the use of the composition to treat spinal cord injury (Answer 8). To make up for this deficiency, the Examiner relies on Edwards to teach "that spinal cord fracture and injury always cause[s] pain" (*id.*). More specifically, Edwards teaches that a

> fractured spine deforms the human structure to varying extents, creating various degrees of instability and always causing pain. The more severe the injury, the more likely the possibility of spinal cord damage. When the spinal cord is injured, the ramifications can range from simple contrusion [sic] to various stages of neurological damage and finally, to complete, irreparable spinal cord injury.

(Edwards, col. 7, ll. 11-19.) According to Appellants' Specification a "wide variety of injuries may be treated in the present invention. In various forms

of the invention, the injury may arise from a compression or other contusion of the spinal cord, crushing of the spinal cord or severing of the spinal cord" (Specification 14: 21-24).

Based on this evidence the Examiner concludes that it "would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the PEG containing composition of Shulman in the treatment of spinal cord fractures and injury" (Answer 9).

Claim 22.

Appellants argue that "Shulman teaches polyethylene glycol solely as a suspending agent in a composition to be injected for pain relief" (Br. 18). Appellants also argue that Edwards is silent as to polyethylene glycol or C1-C10 polyalkylene glycols in general (Br. 19). "While Appellants do not deny that spinal fractures and deformities likely cause pain, Appellants submit that there is no suggestion or motivation to combine the disclosure of Shulman with that of Edwards" (Br. 20).

Therefore, the issue before use is two-fold. Does the combination of Shulman and Edwards teach a method wherein an injured spinal cord is contacted with an amount of at least one C1-C10 polyalkylene glycol, or PEG? If so, is the restoration of nerve impulse conduction through the injured spinal cord simply the discovery of a new benefit of the method taught by Shulman?

Appellants concede that Shulman teaches the use of a composition comprising PEG to treat pain and that spinal fractures likely cause pain. Edwards teaches that spinal fractures always cause pain and severe spinal fractures may result in spinal cord injuries that range from a simple

contusion to irreparable spinal cord injury. Appellants do not dispute and therefore concede that the spinal cord injuries disclosed by Edwards, e.g., contusions, are spinal cord injuries within the scope of their claimed invention. Appellants do not dispute, and therefore concede, that the molecular weight of the PEG taught by Shulman is within the scope of their claimed invention. Appellants also do not dispute, and therefore concede, that Shulman contacts a spinal cord with a composition comprising 2.3% or up to 10% PEG having a molecular weight that is within the scope of their claimed invention. Further, Appellants do not dispute, and therefore concede, that Shulman suggests the administration of the composition to alleviate pain within a period no greater than about 24 hours after injury.

Thus, the preponderance of the evidence supports a finding that a person of ordinary skill in the art would recognize the use of Shulman's composition that comprises up to 10% PEG to treat, by epidural injection, the pain associated with a vertebral fracture resulting in spinal cord injury, e.g., a contusion. Thus, the combination of Shulman and Edwards teach a method wherein an injured spinal cord is contacted with an amount of at least one C1-C10 polyalkylene glycol, or PEG.

While Appellants' Specification discloses that "the composition typically includes at least about 40% of the fusion agent by weight, more preferably about 40% to about 50% by weight, and most preferably about 50% to about 55% by weight", Appellants' Specification discloses that "the percent by weight of the fusion agent in the composition may vary" (Specification 12: 20-23). There is no evidence on this record to suggest that a concentration of up to 10% PEG is ineffective to restore nerve impulse conduction through the injured spinal cord.

In this regard, we note that Appellants' Specification discloses that "[t]he efficacy of the treatment may be determined in a variety of ways" (Specification 14: 25-26) and that "[n]erve function is considered to have been at least partially restored if there is an increase in the conduction of action potential after treatment" (Specification 14: 30-31), or "there is an increased reflex behavior after treatment" (Specification 15: 16-17). There is no evidence on this record to suggest that the phrase "restore nerve impulse conduction", as it appears in claim 22, must be interpreted to mean a complete restoration of nerve impulse conduction through an injured spinal cord, or even a substantial restoration. Claim 22 reads on any increase in the conduction of action potential or increase in reflex behavior after treatment.

In the absence of evidence to the contrary, of which there is none, we find that the administration, by epidural injection, of Shulman's composition comprising up to 10% PEG to an injured spinal cord for the treatment of pain would have resulted in the restoration of nerve impulse conduction through the injured spinal cord. Therefore, we conclude that Appellants have simply discovered a new benefit of the method taught by Shulman. *Woodruff*, 919 F.2d at 1578.

Accordingly, we affirm the rejection of claim 22 under 35 U.S.C § 103(a) as unpatentable over the combination of Shulman and Edwards. Claims 23-29, 38, 39, and 44 fall together with claim 22.

Claim 30:

"Appellants submit that neither Shulman nor Edwards provide[s] any teachings or suggestions of 4-aminopyridine" (Br. 12). We agree.

Accordingly, we reverse the rejection of claims 30, 40, and 43 under 35 U.S.C § 103(a) as unpatentable over the combination of Shulman and Edwards.[4]

CONCLUSION

In summary, we reverse rejection 1 and rejection 2. As to rejection 3, we affirm the rejection of claims 22-39, 38, 39, and 44; and reverse the rejection of claims 30, 40, and 43.

AFFIRMED-IN-PART

Ssc

MUETING, RAASCH & GEBHARDT, P.A.
P.O. BOX 581415
MINNEAPOLIS, MN 55458

[4] We recognize the Examiner's reliance on Potter to teach "the use of 4-aminopyridine to treat spinal cord injury" (Answer 7). Before any further action is taken on the merits, we encourage the Examiner to take a step back and consider whether Potter can be properly combined with the combination of Shulman and Edwards.